Responding to the Anthrax Crisis

Occupational Safety and Health Branch, DS, ORS

National Institutes of Health

Applied Research Portfolio

[redacted]

[redacted]

Why Has OSHB Become Involved in These Efforts?

- Support for emergency response personnel
- Response to NIH personnel's safety and health concerns
- Environmental sampling in mail handling facilities
- Microbiological screening of suspicious mail
- Inadequacy of Level A Laboratory response capabilities

Why Has OSHB Become Involved in These Efforts? (Cont.)

- Development of a surrogate system for "weaponized" anthrax
- Inadequacy of standard Biological Indicators (BIs)
- Lack of enhanced or "weaponized" biological indicators

Why Has OSHB Become Involved in These Efforts? (cont.)

- Standardization of environmental sampling procedures
- Informal consultation with Dept. of State-Sterling SA-32
- Mail decontamination efforts
- Identification of chlorine dioxide as a viable decontamination method for mail (leading to partnering with CDG)

OSHB Applied Research Portfolio

- Comparison and standardization of environmental sampling techniques
- Expansion of Level A Laboratory capabilities-addition of commercial biochemical and monoclonal antibody technologies
- Development of the enhanced or "weaponized" anthrax surrogate system

OSHB Applied Research Portfolio (cont.)

- Generational mail cross-contamination experiments
- Decontamination of mail with high purity chlorine dioxide gas
  (in partnership with CDG)
- Development of enhanced biological indicators (in partnership with CDG)

The Team

NIH

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CDG

- Thomas E. McWhorter, *President and CEO*
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KILLING "*WEAPONIZED*" ANTHRAX

Briefing of TSWG

by

Occupational Safety and Health Branch, DS, ORS

[redacted]

Introduction

US facilities and mail have been contaminated with Anthrax spores; they must be decontaminated.

In conventional sterilization, benign spores (*B. subtilis*) are used as surrogates (biological indicators, BI) for pathogenic spores (Anthrax).

The Anthrax spores of recent events have been "weaponized"– they are finely dispersed and small (<5 μ), highly concentrated (~10^{12}) and aerosolize easily

Weaponization changes the spores' susceptibility to sterilization regimes—it makes them harder to kill.

Commercial *B. subtilis* BI's may not be appropriate surrogates for weaponized Anthrax spores. Inactivation commercial indicators does not permit concluding that "weaponized" anthrax has been killed.

Introduction

"Weaponization" (enhancement)—the ability to produce finely dispersed, highly concentrated, easily aerosolized, and sterilization-resistant spores– is a frighteningly simple process.

NIH/CDG have prepared "weaponized" *B. subtilis* BI's (*WBI*s), which are much harder to kill than commercial BI's, and which are proposed as appropriate surrogates for weaponized Anthrax.

Standard steam, EtO, formaldehyde and chlorine dioxide sterilization regimes are not effective against *WBI*s.

Special cycles (developed by CDG) using high-purity chlorine dioxide gas, have proved effective at killing *WBI*s. NIH has overseen the work, and performed the microbiological analyses.

Weaponization

The "weaponizing" Process:

- Concentrated spores are milled
- Ingredients added/ surfaces modified
  - **Reverses the charge on spores**
  - **Selectively & strongly hydrophilic, protecting spores from re-hydration**
  - **May initiate the activation signal preparing the spore for germination**

The "weaponized" product:

10^{10}-10^{12} spores per gram;

may be aerosolized and re-aerosolized;

1x3μ geometry (~ asbestos) means likely that low dose required

The ease with which spores can be weaponized poses a continuing threat resulting in the need for continuing surveillance and countermeasures.

Weaponization

NIH testing: WBI^{6} *vs.* WBI^{10} *vs.* Conventional BI^{6}
(superscript reflects # spores /strip)

Results: Conventional BI are *not* equivalent to WBI

Practical implications for ongoing decontamination work:

1. The Hart Building
2. Decontamination protocols—for mail and facilities--*must* use cycles developed and validated against enhanced surrogate challenges, using precise parameters that are properly controlled and documented. WBI use is indicated.
3. Decontamination *is feasible*, *if* properly carried out.

CDG

Background:

DH Rosenblatt– Edgewood Arsenal; Ft. Detrick (1960s)

Gordon, Kieffer & Rosenblatt (1972)

AA Rosenblatt et al– ClO_2 gas for R_x sterilization (~1980)

J&J– Purchases ClO_2 gas:R_x sterilization patents (1990)

CDG: ClO_2 for drinking water treatment (1992-)

CDG/DARPA: ClO_2 gas for facilities decon (2000-)

CDG

Current Work:

- USPS Mail decontamination (proposed)
- *SafeMail*™ Systems (in development)
- USPS facilities decontamination (proposed)

- *WBI* ^{X}: Development of indicators to simulate high-concentration, sterilization-resistant weaponized spores (in partnership with OSHB,NIH)

- Development and validation of cycles for the reliable, reproducible destruction of weaponized spores

CDG

Cycle development & validation:

Procedures and practices used for sterilization of medical devices

Statistical model, based on initial bio-burden and "log" kill.

Parameters ***must*** be precisely controlled and measured.

ClO_2 gas ***must*** be pure.

Critical process variables:

ClO_2 concentration; time; temperature; relative humidity; pressure; mass transfer

Other issues:

Materials compatibility (ClO_2 *vs.* Cl_2)

Effect of Light

Validation/reproducibility of results.

Parametric release– why correlated BIs are essential

CDG
Gas:Solid Technology

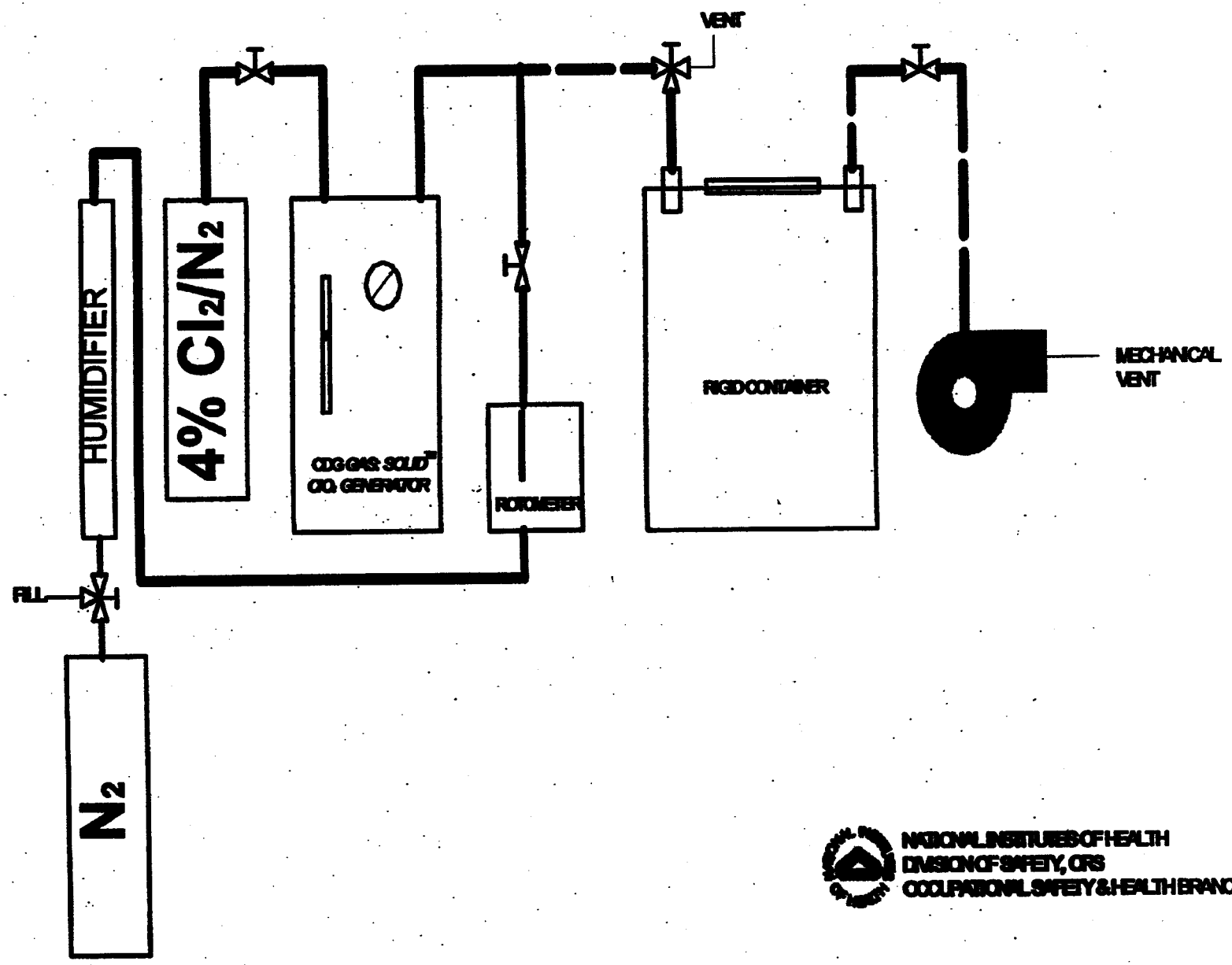
$$Cl_{2\ gas} + NaClO_{2\ solid} \rightarrow 2ClO_{2\ gas} + NaCl_{solid}$$

Pure chlorine dioxide gas (~8%, in nitrogen)

Precise, flexible control

Safe, simple operation.

Uses *Saf-T-Chlor*™ thermally stable solid sodium chlorite.



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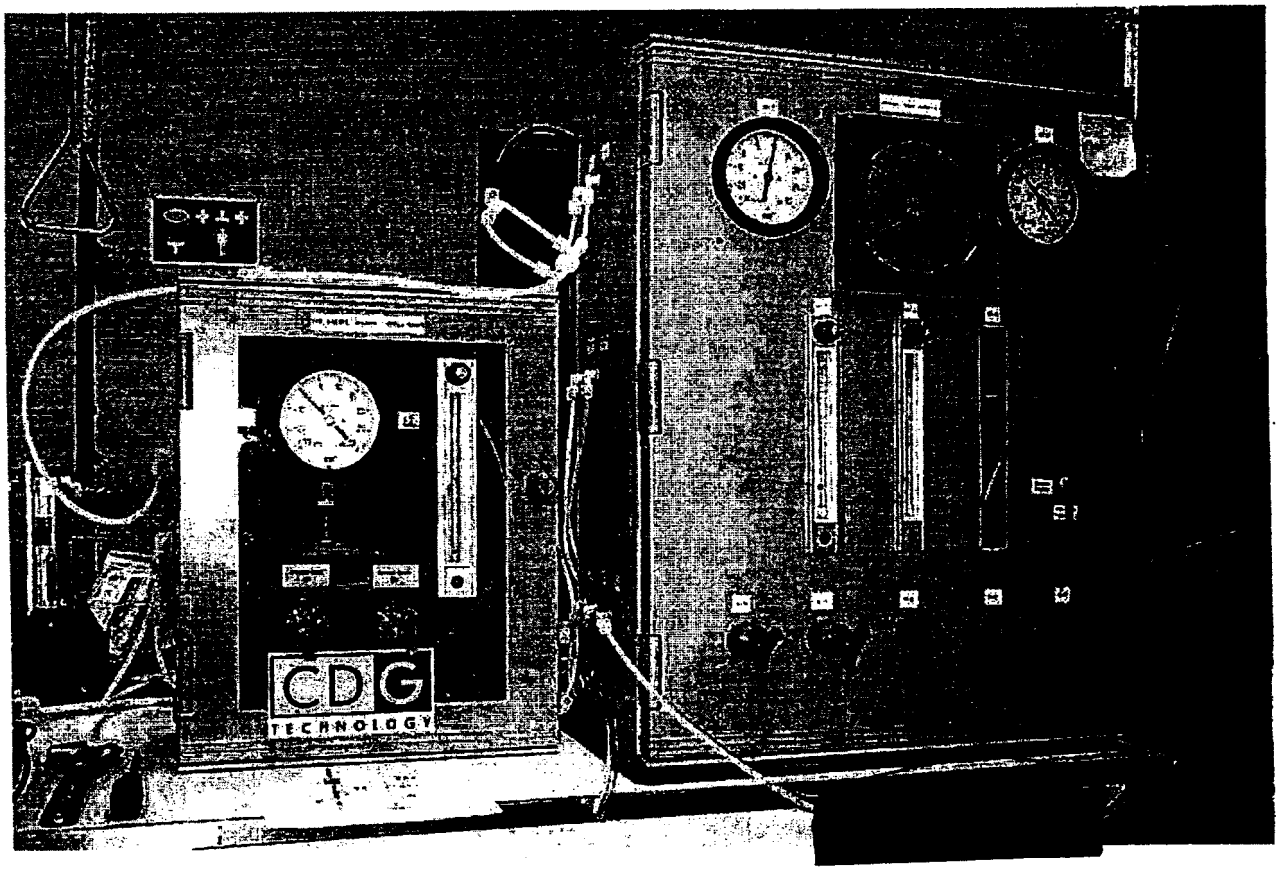
OCCUPATIONAL SAFETY & HEALTH BRANCH

CDG Laboratory
Mail Process Reactor

CDG Laboratory
ClO_2 Generator and Process Controller



CDG Laboratory Humidification Chamber

Practical Implications for Decontamination

Facilities:

Competent preparation of the physical premises is required.

Humidity control is essential to killing pathogens and minimizing damage

Relatively-high gas concentrations are required

Pure ClO_2 minimizes damage, allows for accurate gas measurement

Mass transfer is relatively straightforward

Coherent measurement/documentation of all parameters is essential

Mail:

Pressure vessel is required

Pure ClO_2 ,generated by *gas:solid* technology minimizes damage, allows for accurate gas measurement

Gas consumption is relatively minor

Mass transfer is critical

Coherent measurement/documentation of all parameters is essential

Mail Decontamination with High-Purity Chlorine Dioxide Gas

- 10,000 ppm ClO_2
- 4 hr treatment cycle
- Challenge 2.0×10^8 enhanced spores on swabs
- 16 separate tests (12/13/01-1/4/02)
- Results:
  - 0/16 positive indicating total kill at 10^8

Mail Decontamination with High-Purity Chlorine Dioxide Gas

Effect of Pre-humidification

- 10,000 ppm
- 4 hr treatment
- > 95% relative humidity; 95° F
- Varying humidification times
- Enhanced spores- 2.0×10^8 in sealed envelopes

Effect of Pre-humidification Time on Sterilization of Enhanced Spores with ClO_2 Gas

Humid. Time	1 hr	2 hr	3hr
$2x10^8$ Swab	0/2	0/2	0/2
WBI^{10}	0/2	0/2	0/2
$BI-10^6$	0/2	0/2	0/2
Pos. Control	$1.7x10^8$	$1.7x10^8$	$1.7x10^8$

Mail Decontamination with High-Purity Chlorine Dioxide Gas

Effect of Gas Concentration

- 4 hr treatment
- 1.5 hr pre-humidification
- > 95% relative humidity; 95° F
- Varying humidification times
- Enhanced spores- 2.0×10^8 in sealed envelopes

Effect of Gas Concentration on Sterilization of Enhanced Spores with ClO_2

ClO_2 Conc.	2500 ppm	1000 ppm	500 ppm
$2x10^8$ Swab	0/2	0/2	2/2 $1.43x10^3$
WBI[10]	0/2	0/2	2/2
BI-10^6	0/2	0/2	0/2
WBI[6]			3/4
Pos. Control	$1.7x10^8$	$1.7x10^8$	$1.7x10^8$

Comparison of Biological Indicators at 500ppm ClO_2

Humidification Time	1 hr	2 hr	3hr
WBI[6]	Pos	Pos	Pos
BI-10[6]	Neg	Neg	Neg
WBI[6] Pos. Control	Pos	Pos	Pos
BI-10[6] Pos. Control	Pos	Pos	Pos

WBI^{10} vs. Commercial $BI\text{-}10^{6}$
Efficacy of Steam Sterilization

- 15 min
- 121° C
- 20 psi

<u>Results</u>

(after 15 hr incubation in thioglycollate broth)

- WBI^{10} Heavy growth with pellicle formation
- $BI\text{-}10^{6}$ No growth

Summary

- Weaponized Anthrax poses a unique decontamination challenge.
- Standard BIs are unsuitable surrogates for weaponized spores.
- *WBI*s are proposed as suitable surrogates for weaponized spores.
- Weaponized spores are resistant to standard sterilization regimes.
- It is should be possible to kill weaponized Anthrax-- in mail and in contaminated facilities-- using proven, reliable, commercially available ultra-pure chlorine dioxide gas technology.

Next Steps
Scientific Research

- Replicate testing of WBI^{6} and WBI^{10} for statistical significance
- Development, testing of WBI^{12}
- Mass transfer experiments
- Quality assurance

Next Steps

Process Development & Engineering

- Cycle Optimization:
  Time, Temperature, Humidity, Pressure & Gas Concentration
- Design & Fabrication of Full-scale System
- Logistics, Equipment Shakedown
- Quality Control
- Safety Review

Next Steps
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TSWG